



# AN OVERVIEW OF SUSTAINED RELEASE MATRIX SYSTEM

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## ABSTRACT-

Sustained drug delivery systems are one of the most important techniques for reducing pharmacological side effects by preventing the drug's therapeutic concentration level in the body from fluctuating. The main goals of a sustained drug delivery system are to increase the utility of a drug by optimizing its biopharmaceutical, pharmacokinetic, and pharmacodynamics properties in order to maximize efficiency, reduce adverse effects, and cure the condition. Sustained release drug delivery improves patient compliance by reducing drug administration frequency, lowering steady-state drug levels, increasing the safety margin of low therapeutic index drugs, maximizing drug utilization, and lowering healthcare costs through improved therapy and a shorter treatment period. Tablets are the most cost-effective type of continuous and controlled release dose. Matrix tablets are a useful tool for administering oral extended-release medication. By dispersing solid particles within a porous matrix made of hydrophilic and hydrophobic polymers, matrix tablets can be made using wet granulation or direct compression processes. The availability of various kinds of polymers for managing drug release has become the most essential aspect of matrix tablet composition. Both dissolution-controlled and diffusion-controlled processes are used to release drugs from matrix drug delivery devices.

**KEYWORDS-** Sustained Release, Matrix Tablet, Polymers, Advantages & Disadvantages.

## I. Introduction-

The oral route is the most popular route used for administration of drugs, which is due in part to the ease of administration and to the fact that gastrointestinal physiology offers more flexibility in dosage form design than most other routes. The terms Sustained release, prolonged release, modified release, extended release or depot formulations are used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.

Matrix system is widely used for the purpose of sustained release. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed. In fact, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. The goal of an extended release dosage form is to maintain therapeutic drug level in plasma for extended period of time. [1]

The ideal drug delivery systems have two things would be required first it would be a single dose the duration of treatment whether it is for days or week, as with infection, or for the life time of the patient, as in hypertension or diabetes. Second it should deliver the active entity directly to the site of the action, thereby minimizing side effects. [2]

Sustained drug delivery system is one of the most useful tools that providing promising approaches to decrease the side effect of drug by preventing the fluctuation of the therapeutic concentration level of the drug in the

body. The basic goals of sustained drug delivery system are to optimize the biopharmaceutical, pharmacokinetic and pharmacodynamics properties of a drug in order to maximize the utility, such a way that efficiency is maximized, reduced the side effects and cure of the disease is achieved.

Sustained release drug delivery is improve patient compliance by reduction frequency of drug administration, reduction steady-state fluctuation of drug levels, increased safety margin of low therapeutic index drug, maximum utilization of the drug, reduction in healthcare costs through improved therapy and shorter treatment period.

Matrix tablets may be formulated by wet granulation or direct compression methods by dispersing solid particles within a porous matrix formed of hydrophilic and hydrophobic polymers. The availability of different classes of polymers in controlling the release of drugs has become the most important aspect in the formulation of matrix tablets. The release of drug from matrix drug delivery systems by both dissolution-controlled as well as diffusion controlled mechanisms. [3]

The oral route of administration for sustained release systems has received greater attention because of more flexibility in dosage form design. The design of oral sustained release delivery systems is subjected to several interrelated variables of considerable importance such as the type of delivery system, the disease being treated, the patient, the length of therapy and the properties of the drug. [4]

## II. THE RATIONALE FOR DEVELOPING SUSTAINED RELEASE

1. To extend the duration of action of the drug.
2. To minimize the fluctuation in plasma level.
3. To reduce the frequency of dosing.
4. Improved drug utilization.
5. Less adverse effects.
6. To scale down the frequency and inter and intra subject variability.
7. To reduce the fluctuations in plasma level and drug toxicity.
8. To reduce cost of treatment. [4, 13]

## III. ADVANTAGES OF SUSTAIN RELEASE DOSAGE FORMS-

1. Reduction in frequency of intakes.
2. Reduce side effects.
3. Uniform release of drug over time.
4. Better patient compliance
5. Reduced drug plasma level fluctuation.
6. Reduction the total dose.
7. Improvement of deficiency in treatment.
8. Reduction the cost of treatment.
9. Control of drug therapy is achieved.
10. Rate and extent of drug absorption can be is modified.
11. Drug administration can be made convenient [11, 14, 15]

## IV. DISADVANTAGES OF SUSTAINED RELEASE DRUG DELIVERY –

1. Increased cost.
2. Toxicity due to dose dumping.
3. Unpredictable and often poor in vitro-in vivo correlation.
4. Risk of side effects or toxicity upon fast release of contained drug.
5. Increased potential for first- pass clearance.
6. Need for additional patient education and counseling.
7. Dose dumping may occur with the faulty formulation.
8. More cost than conventional dosage form.
9. Reduced potential for dose adjustment.
10. Increased potential for first-pass metabolism. [2, 19, 20]

## V. Methods of preparation

**1. Direct Compression** -In this process powdered materials are compressed directly without changing the properties of the drug like physical and chemical properties.

### 2. Wet Granulation -

In this method weighed quantities of drug and polymer are mixed with sufficient volume of granulating agent. After enough cohesiveness was obtained, then screening of wet mass. The granules are dried and screening of dry granules, then blending with lubricant and disintegrant to produce “running powder” tablets are compressed using a single-punch tablet compression machine.

### 3. Melt Granulation -

In this process use of a substance, which melts at relatively low temperature. This substance can be added in the molten form over the substrate, which is then heated above its melting point. Different lipophilic binders were tried by using melt granulation technique.

### 4. Hot-Melt Extrusion Process -

In the hot-melt extrusion process, a mixture of the active ingredients, the thermoplastic polymers and other processing aids is fed into the barrel of the extruder through the hopper. The materials are transferred inside the heated barrel by a rotating screw.

The materials melt at elevated temperatures and the molten mass is continuously pumped through the die attached at the end of the barrel. Depending upon the dimensions of the die cylinders, films can also be produced from the extruder. [6, 30]

## VI. MATRIX TABLET

Matrix tablets can be defined as the oral solid dosage forms in which the drug is homogeneously dispersed or dissolved within the hydrophilic or hydrophobic polymeric matrices. The preparation of sustained release matrix tablets involves the direct compression of blend powder mixture of drug, retardant material and other additives to formulate a tablet in which the drug is dispersed in a matrix of the retardant. Alternatively, drug, retardant blend and other additives may be granulated prior to compression. These systems release the drug in a continuous manner by dissolution-controlled and diffusion-controlled mechanisms. Hydrophilic polymer matrix is extensively used for formulating an SR dosage form [4]

## VII. ADVANTAGES OF SR MATRIX DDS

1. The frequency of drug administration is reduced.
2. Patient compliance can be enhanced.
3. Drug administration can be made more suitable as well.
4. The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced.
5. Better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a dose of a high availability drug can be reduce.
6. The characteristic blood level variations due to multiple dosing of conventional dosage forms can be reduced.[18,4]

## VIII. DISADVANTAGES OF SR MATRIX DDS

1. Probability of dose dumping.
2. Reduced potential for dose adjustment.
3. Cost of single unit higher than predictable dosage forms.
4. Increase potential for first pass metabolism.
5. Requirement for additional patient education for proper medication. [18, 4]

## IX. TERMINOLOGY-

The following are some of the terms that have been used to describe long-term medication delivery systems

1. Modified release dosage forms – Those dosage forms whose drug release features of time course and/or location are intended to achieve therapeutic and/or convenience goals that conventional dosage forms do not provide. [24]
2. Controlled release- The medication is delivered at a constant (zero order) rate, and the drug concentration after delivery is time invariant. [25]
3. Delayed release- The medicine is released at a different time than when it was given.
4. Extended release- The medicine is released slowly such that plasma concentrations remain at therapeutic levels for a long time, usually between 8 and 12 hours. [26]
5. Prolonged release-The medicine is given in a dose form that allows it to be absorbed over a longer length of time than a traditional dosage form. However, there is a possibility that onset is delayed as a result of the dose form's general slower release rate. [27]
6. Repeat action- Indicates that a single dose is delivered quickly after administration, and that second and third doses are released at irregular intervals. [28]
7. Sustained release- The medicine is released slowly, according to the delivery system's specifications.[29]

## X. Criteria for Drug Candidate for formulation of oral sustained release systems-

The route of administration, the type of delivery system, the ailment being treated, the patient, the length of therapy, and the qualities of the drug all influence the design of a sustained release system. These are either the drug's physicochemical or biological characteristics.

## XI. PHYSIOCHEMICAL PROPERTIES-

1. **Dose size-** In general, a single oral dose of 0.5-1.0 gm is considered the maximum for a traditional dosage form. This is likewise true for long-acting dose types.
2. **Aqueous solubility** – Drugs having a very low solubility (less than 0.01 mg/ml) have a high probability of being sustained. Because 0.1 mg/ml is considered the bottom limit for a drug's solubility in a sustained-release system, the drug's solubility will limit the mechanism used in the system.
3. **Partition coefficient-** The medicine must traverse a variety of biological membranes between administration and excretion from the body in order to have a therapeutic impact in another part of the body. Drugs having a low partition coefficient pass through biological membranes with ease. Drugs having a high partition coefficient will easily enter the membrane, causing a buildup in bodily tissue and a sluggish removal.
4. **Stability-**Orally given drugs are susceptible to acid-base hydrolysis as well as enzymatic degradation. For medications that are unstable in the stomach, systems that prolong delivery over the complete course of transits in the GI tract are helpful. When supplied from a sustaining source, drugs that are unstable in the small intestine may have lower bioavailability. This is due to the fact that more medications are administered in the small intestine, where they are more likely to be degraded.
5. **Protein binding-** Many medications can bind to plasma proteins, affecting the duration of the drug's activity. Drug binding to a protein can act as a depot for the drug, resulting in a protracted release profile, especially if there is a significant degree of drug binding. [19]

## XII. BIOLOGICAL PROPERTIES:

**1. Biological Half-Life-** Because sustained release formulations can minimize dose frequency, active therapeutic medicines with short half-lives are ideal choices. Drugs with half-lives less than 2 hours are generally not good candidates for sustained-release formulations. Drugs with large half-lives (more than 8 hours) are rarely employed in sustained release formulations since their action is already long-lasting.

**2. Absorption** – The absorption rate constant is a fictitious rate constant that should be the drug's release rate constant from the dose form. Drugs with real reduced absorption rate constants will not be good candidates for keeping the system running.

**3. Distribution** - Drugs with a large apparent volume of distribution, which affects the pace of drug clearance, such as chloroquine, are not good candidates for oral sustained release formulations.

**4. Metabolism** –Slower-releasing dose forms can have poorer bioavailability due to drug metabolism before absorption, either in the lumen or tissue of the intestine. The majority of intestinal enzyme systems are saturable. Because the medication is released at a slower pace in these areas, there is less total drug presented to the enzymatic process over time, allowing the drug to be completely converted to its metabolites. [19]

## XIII. CLASSIFICATION OF MATRIX TABLETS:

### On the Basis of Retardant Material Used:

Matrix tablets can be divided in to 5 types -

#### 1. Hydrophobic Matrices (Plastic matrices):

In 1959, the idea of using hydrophobic or inert materials as matrix materials was suggested for the first time. The medicine is combined with an inert or hydrophobic polymer and then compacted into a tablet in this approach of generating sustained release from an oral dosage form. The dissolving medication diffuses through a network of channels that exist between compressed polymer particles, resulting in sustained release. Polyethylene, polyvinyl chloride, ethyl cellulose, and acrylate polymers and copolymers are examples of materials that have been employed as inert or hydrophobic matrices. Liquid penetration into the matrix is the rate-controlling stage in these formulations. Diffusion is one probable mechanism for drug release in these types of tablets. In the presence of water and gastrointestinal fluid, such matrix tablets become inert.

**2. Lipid Matrices:** Lipid waxes and other components were used to create these matrices. Both pore diffusion and erosion are used to release drugs from these matrices. As a result, the digestive fluid composition is more sensitive to release characteristics than the completely insoluble polymer matrix. Many prolonged release formulations have used carnauba wax in combination with stearyl alcohol or stearic acid as a retardant base.

**3. Hydrophilic Matrices:** Because of their flexibility in achieving a desired drug release profile, cost effectiveness, and broad regulatory acceptability, hydrophilic polymer matrix systems are widely utilised in oral controlled drug delivery. The use of hydrophilic polymers with high gelling capabilities as base excipients in the formulation of pharmaceuticals in gelatinous capsules or, more often, tablets, is of special relevance in the field of controlled release. A well-mixed combination of one or more medications with a gelling agent is characterised as infecting a matrix (hydrophilic polymer). Swellable controlled release systems are the name for these systems. The polymers used to make hydrophilic matrices can be categorised into three categories.

**A. Cellulose derivatives:**

Methylcellulose 400 and 4000cPs, hydroxy ethyl cellulose; hydroxy propyl methyl cellulose (HPMC) 25, 100, 4000 and 15000cPs; and Sodium carboxy methyl cellulose.

**B. Non cellulose natural or semi synthetic polymers:**

Agar-Agar; Carob gum; Alginates; Molasses;

Polysaccharides of mannose and galactose,

Chitosan and Modified starches.

**Polymers of acrylic acid:**

Polymers which are used in acrylic acid category is Carbopol 934. Other hydrophilic materials used for preparation of matrix tablet are Alginic acid, Gelatin and Natural gums.

**Fat-wax matrix tablet:**

Spray congealing in air, blend congealing in an aqueous media with or without surfactant, and spray-drying procedures can all be used to integrate the medication into fat wax granulations. A suspension of medication and melted fat-wax is allowed to solidify and then comminuted for sustained-release granulations in the bulk congealing process. By compacting with a roller compactor, heating in a suitable mixture such as a fluidized-bed and steam jacketed blender, or granulating with a solution of waxy material or other binders, the mixture of active substances, waxy materials, and fillers can also be transformed into granules. Leaching and/or hydrolysis, as well as fat dissolution under the effect of enzymes and pH changes in the gastrointestinal tract, release the medication embedded in a melt of fats and waxes. Surfactants can affect both the drug release rate and the fraction of total drug that can be incorporated into a matrix by adding them to the formulation.

**4. Biodegradable Matrices:**

These are polymers that are made up of monomers connected together by functional groups and have a backbone with an unstable bond. They are biologically destroyed or eroded into oligomers and monomers that can be metabolised or expelled by enzymes produced by surrounding living cells or by non-enzymatic processes. Natural polymers like proteins and polysaccharides, as well as modified natural polymers and synthetic polymers such aliphatic poly (esters) and poly anhydrides, are examples.

**5. Mineral Matrices:** These are made up of polymers derived from several seaweed species. Alginic acid, for example, is a hydrophilic carbohydrate produced by dilute alkali from brown seaweed species (Phaeophyceae) [1]

**XIV. POLYMERS**

Polymers, unlike low-weight molecular compounds, are complicated and large molecules with carbons forming the backbone. Monomers are singular repeating units/molecules that are tiny in size. A copolymer or homopolymer is a polymer made up of two distinct monomers. Low density, good corrosion resistance, low cost, poor temperature resistance, and translucent or coloured are some of its properties.

**Polymers used in Matrix tablets****a) Hydrogels**

Polyhydroxyethylmethacrylate (PHEMA), Cross-linked polyvinyl alcohol (PVA), Crosslinked polyvinyl pyrrolidone (PVP), Polyethylene oxide (PEO), Polyacrylamide (PA).

**b) Soluble polymers**

Polyethylene glycol (PEG), polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), Hydroxypropyl methyl cellulose (HPMC).

**c) Biodegradable polymers**

Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PCL), Polyanhydrides, Polyorthoesters

**d) Non-biodegradable polymers**

Polyethylene vinyl acetate (PVA), Polydimethylsiloxane (PDS), Polyether urethane (PEU), Polyvinyl chloride (PVC), Cellulose acetate (CA), Ethyl cellulose (EC)

**e) Mucoadhesive polymers**

Polycarboxophil, Sodium carboxymethyl cellulose, Polyacrylic acid, Tragacanth, Methyl cellulose, Pectin

**f) Natural polymers in sustained release drug delivery**

Xanthan Gum, Guar Gum, Sodium Alginate, Pectin, Chitosan. [5]

**XV. DRUG RELEASE MECHANISM FROM SR MATRIX DDS****Zero Order Kinetics -**

A zero order release would be predicted by the following equation,  $Q_t - Q_0 = K_0t$

Where,  $Q_t$  = Amount of drug release dissolved in time 't'.  $Q_0$  = Initial amount of drug concentration in solution.  $K_0t$  = Zero order rate constant.

When the data was plotted as cumulative % drug release verses time, if the plot is linear then data obeys zero order kinetics with slope equal to  $K_0$ . This model represents an ideal release profile in order to achieve the prolonged pharmacological action.

**First Order Kinetics -**

A first order release would be predicted by the following equation  $\log Q_t = \log Q_0 - K_1t/2.303$

Where,  $Q_t$  = Amount of drug released in time 't'.  $Q_0$  = Initial amount of drug concentration in solution.  $K_1t$  = First order rate constant.

When data was plotted as log cumulative % drug remaining verses time yields a straight line indicating that the release follows first order kinetics. The constant  $K$  can be obtained multiplying slope values.

**Higuchi's Model -**

Drug release from the matrix device by diffusion has been described by Higuchi's Diffusion equation  $ft = Q = \sqrt{D\delta/\tau} (2C - \delta C_s) C_{st}$

Where,  $Q$  = Amount of drug released in time 't'.  $D$  = Diffusion coefficient of the drug in the matrix.  $C_s$  = Solubility of the drug in the matrix.  $\delta$  = Porosity of matrix.  $\tau$  = Tortuosity.  $t$  = Time (h).

The equation may be simplified then equation becomes;  $ft = Q = KH \times t^{1/2}$

Where,  $KH$  = Higuchi dissolution constant.

When data was plotted according to this equation, i.e., cumulative drug released verses square root of time, yields a straight line, indicating that the drug was released by diffusion mechanism.

**Peppas Korsmeyer Equation -**

In 1983 Korsmeyer *et al.* (Korsmeyer *et al.*, 1983) developed a simple, semi-empiric model, when diffusion is the main drug release mechanism, relating exponentially the drug release to the elapsed time (t).

$$At/A_\infty = ktn$$

Where,  $k$  = Constant.  $n$  = Release.  $t$  = Time.  $A_t$  and  $A_\infty$  = Absolute cumulative amount of drug released at time 't'.

This is used when the release mechanism is not well known or when more than one type of release phenomenon could be involved.

**Hixon-Crowell Equation -**

Drug released from the matrix device by diffusion has been described by Hixon-Crowell diffusion equation;  $W_0^{1/3} - W_t^{1/3} = Kt$

Where,  $W_0$  = Initial amount of drug.  $W_t$  = Remaining amount of drug.  $t$  = Time.  $K$  = Constant (Kappa).

This expression applies to pharmaceutical dosage form such as tablets where the dissolution occurs in planes that are parallel to drug surface if tablet dimensions diminish proportionally in such manner that the initial geometrical form keeps constant all the time. [12,23]

**Classification**

The most common methods used to achieve sustained release of orally administered drugs are as follows-

**Diffusion Systems-** The release rate of a drug in a diffusion system is determined by its diffusion through an inert membrane barrier. This barrier is usually made of an insoluble polymer. Diffusional systems can be divided into two categories or subclasses: reservoir devices and matrix devices.

- a) **Reservoir Devices** -Reservoir devices have a drug core and a reservoir surrounded by a polymeric membrane, as the name suggests. The rate of medication release from the system is determined by the type of the membrane. Polymer coatings can also be used to achieve long-term release. The polymer should not disintegrate for this purpose, but rather allow the medication to diffuse through the polymer barrier to the outside, or into the gastrointestinal system in the case of oral drug delivery.

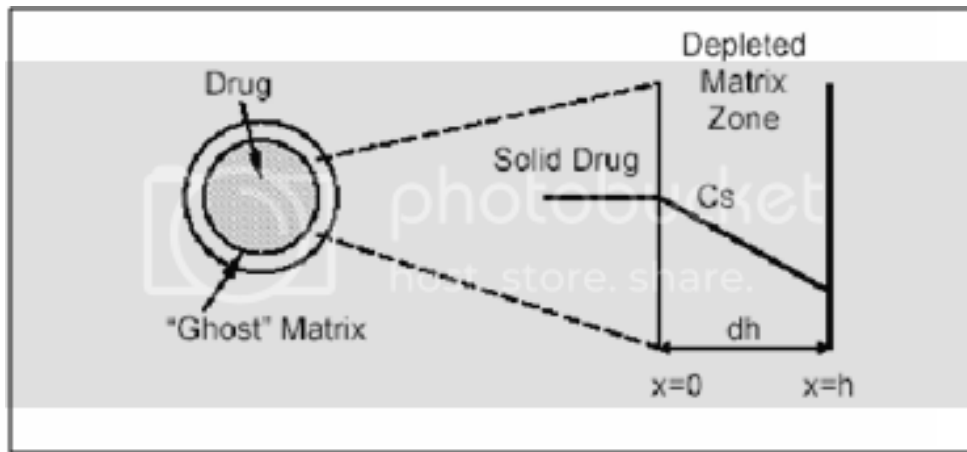


Figure 1 .Schematic representation of a reservoir diffusional device.

### b) Matrix Devices:

As the name implies, a matrix device is made up of medication that is uniformly spread within a polymer matrix. In the model, the medication in the bathing solution-exposed outer layer dissolves first, then diffuses out of the matrix. The interface between the bathing solution and the solid drug continues to move towards the interior. Obviously, for this system to be diffusion regulated, the rate of dissolution of drug particles within the matrix must be significantly faster than the rate of dissolved drug leaving the matrix.

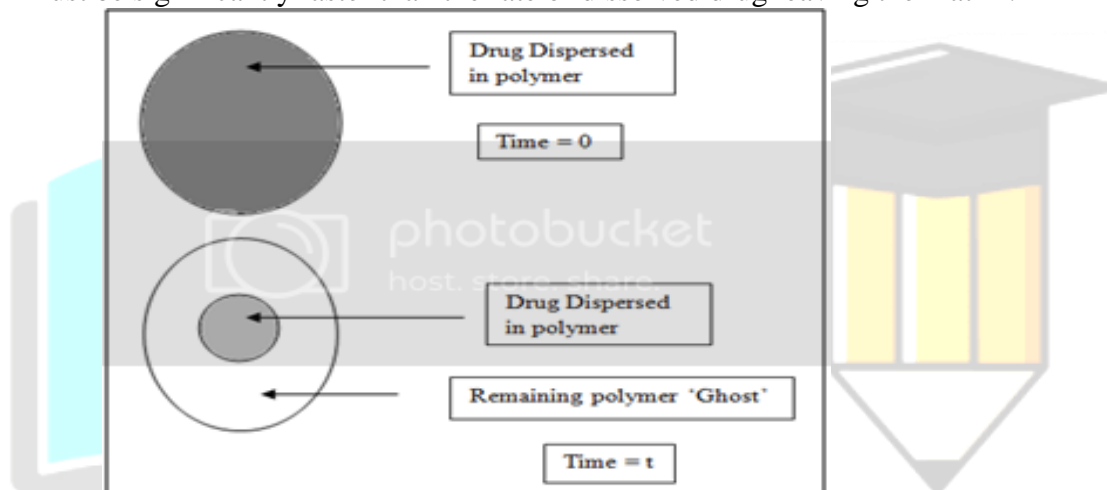


Figure 2. Matrix diffusional system before drug release (time=0) and after partial drug release (time=t).

**Dissolution Systems-** Because the rate of disintegration will limit the amount of drug released, it appears self-evident that a drug with a slow dissolving rate will have sustaining characteristics. Given this, a sustained-release medication might be created by slowing down the rate of disintegration. Preparing appropriate salts or derivatives, coating the medication with a slowly dissolving substance, or integrating it into a tablet with a slowly dissolving carrier are all options for accomplishing this.

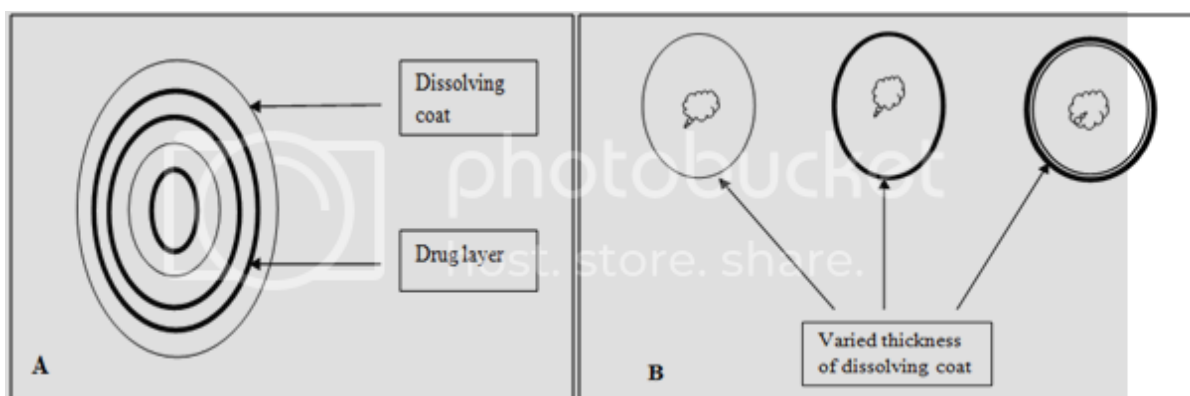


Figure 3. Two types of dissolution-controlled delivery system: (A) single bead type device with alternating drug and rate controlling layer; (B) beads containing drug with differing thickness of dissolving coats.

**Osmotic System**-To maintain a steady release of medication, osmotic pressure is used as a driving factor. Consider a semipermeable membrane that allows water through but not drugs. Water will flow into the tablet when this gadget is exposed to water or any other bodily fluid due to the osmotic pressure difference. These systems are usually found in two different configurations. The first has a solid core with the medicine and an electrolyte that is dissolved by the incoming water. The high osmotic pressure differential is provided by the electrolyte. The medicine is in solution in the second system, which is contained within the device by an impermeable membrane.

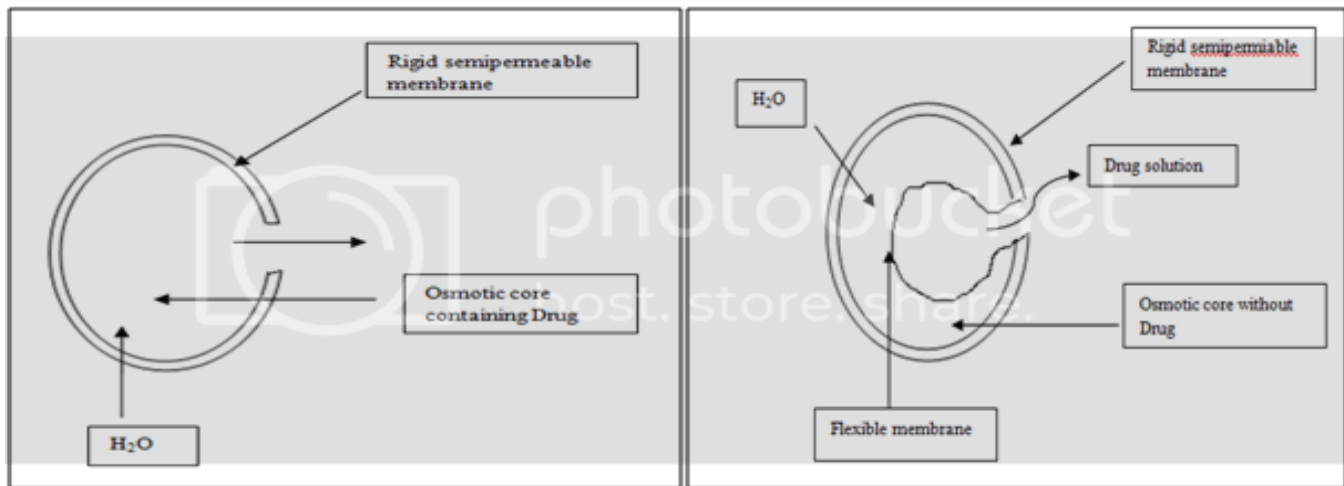
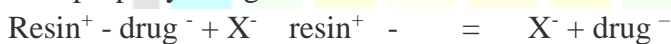


Figure 4. Diagrammatic representation of two types of osmotically controlled system.

**Ion-Exchange Resins**- Resins made up of water-insoluble cross-linked polymers are commonly used in ion-exchange systems. Salt-forming functional groups are found in repeating places on the polymer chain in these polymers. The medication is attached to the resin and released by ion-exchange groups that come into contact with properly charged ions.



Conversely,



The medicine that isn't bound to the resin diffuses out. The drug-resin complex is made by repeatedly exposing the resin to the drug in a chromatography column or by allowing the resin to touch the drug in solution for an extended period of time.

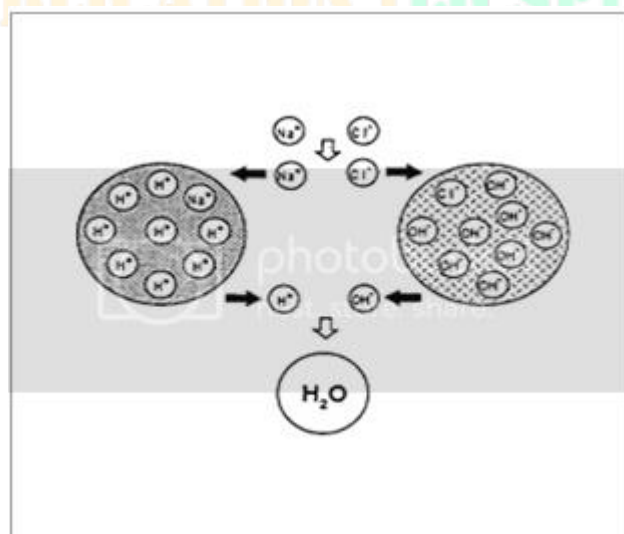


Figure 5. Diagrammatic representation of Ion Exchange resins.

**Swelling and Expansion Systems**- Because of their small pore size, which typically spans from nanometers to low micrometres, traditional hydrogels swell slowly when exposed to water. Swelling is faster and may result in a large rise in size if the hydrogel has a pore size of more than 100 m. It is possible to reach swelling ratios of above 100. These swelled systems grow too massive to pass through the pylorus and are consequently

kept in the stomach even after the housekeeper wave, if they have sufficient mechanical strength to endure the peristaltic movement in the stomach's antrum.

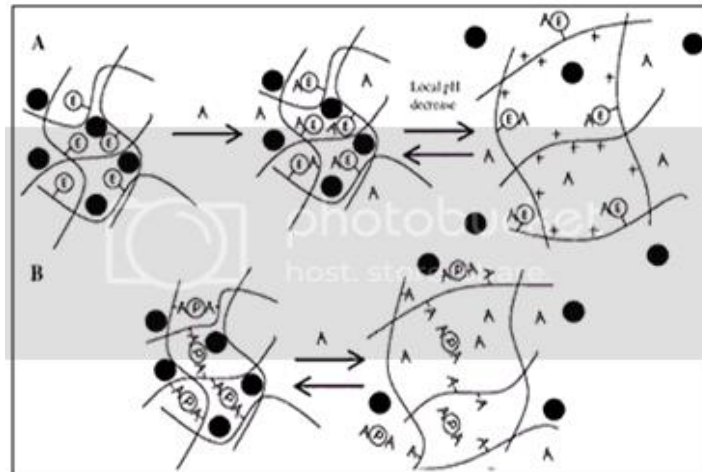


Figure 6. Diagrammatic representation of Swelling and Expansion Systems.

### Floating system-

If the dosage form has a lesser density than the gastric fluids, it will float on top of the contents of the stomach, providing for a longer period for the drug to be released before the system is emptied into the small intestine. The density of stomach fluid is around 1gm/cm<sup>3</sup>. If the dosage form has a lower density than that, it will float in the gastric juices. As previously mentioned, these systems require a certain amount of fluid in the stomach as well as the availability of food. There have been several varieties of low density single-unit (tablets) and multiple-unit (pellets) dosage forms developed. If the density of a dose form is greater than 2.5gm/cm<sup>3</sup>, it will sink to the bottom of the stomach, where pellets may become stuck in the folds of the gastric wall.

### Bioadhesive or Mucoadhesive System:

To accomplish gastric retention, Bioadhesive or Mucoadhesive polymers such as polyacrylic acid and chitosen have been recommended. The underlying concept is that the mucoadhesive or bioadhesive polymers cause the dose forms to adhere to the gastrointestinal mucus. While the bioadhesive or mucoadhesive technique is appropriate for buccal or sublingual formulations, due to the rapid turnover of mucus in the stomach, it is not as simple for gastroretentive systems. Last but not least, magnetic elements can be incorporated to the dosage forms. These systems can then be held in place by an external magnet, however this method necessitates exact positioning of the external magnet and is unlikely to result in high patient compliance. [7, 22]

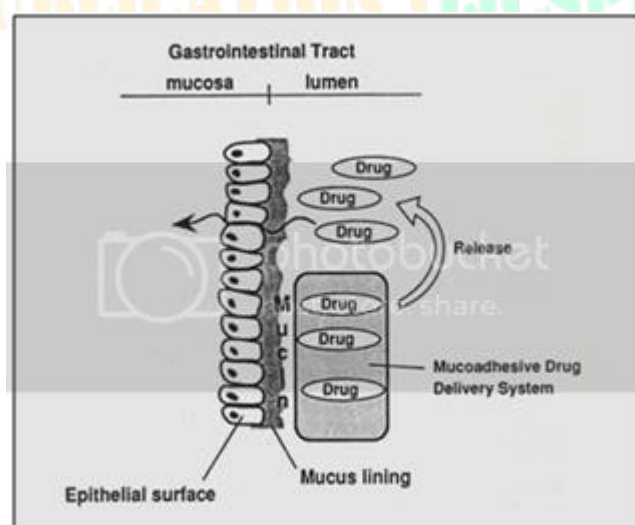


Figure 7. Diagrammatic representation of Bioadhesive or Mucoadhesive systems.

Matrix formulations are defined as a drug or other active ingredient embedded in insoluble excipients in order to achieve release by a continuous leaching of the drug from the inert matrix core.

Matrix systems can be divided into three types:

1. Monolithic matrix tablets

2. Gel forming hydrophilic matrix tablet

3. Erodible (hydrophobic) matrix tablets

**1. Monolithic matrix tablets:** Incorporation of a medication in an inert matrix is probably the easiest approach of generating sustained release of a drug from an oral dosage form. In this context, inert refers to a substance that does not interact with bodily fluids. The fact that drug release from plastic matrix tablets is independent of the state and condition of the digestive juices, which can vary greatly between and within patients, is the fundamental reason for its popularity (pH, viscosity). The porous matrix tablet does not disintegrate like ordinary tablets do during transit through the gastrointestinal tract; instead, it remains intact and the skeleton can be recovered in faeces. The majority of the ingredients utilised to make these inert matrices are (insoluble) polymers and lipophilic chemicals. Polyethylene, polyvinyl chloride, poly methyl methacrylate, polystyrene, poly vinyl acetate, cellulose acetate, and ethyl cellulose were among the first semi-synthetic polymers used to make matrix tablets. Carnuba wax, hydrogenated castor oil, and tristearin were among the fat compounds employed. The inherent first order drug release characteristics of most inert polymeric matrix tablets, as well as their poor direct compression characteristics and the difficult cleaning of agglomeration equipment used to prepare agglomerates with the required compression characteristics, were major drawbacks.

**Mechanism of release of inert monolithic matrix tablets:**

A leaching method is used to release inert matrix tablets. Drug particles dispersed in the polymer matrix dissolve in penetrating gastro intestinal fluids and are released from the tablet by diffusion through a porous network of pre-existing pores and pores generated by the drug particles' dissolution. A continuous structure connecting all drug particles exists at drug loadings greater than 10-15 volume percent (percolating drug network). At even smaller loadings, a specific proportion of the medication (trapped fraction) may be fully enveloped by the polymer matrix, resulting in partial release.

**Solvent activated matrix tablets:** The use of solvent activated matrix tablets to achieve zero order Hoffenberg was the first to propose release, or steady release rates over a long period of time. The term "solvent activated drug delivery system" refers to all systems in which controlled release is achieved by the interaction of polymer and water. Plasticization, swelling, dissolving, erosion, and degradation of the polymer may occur as a result of its interaction with water. Gel-forming hydrophilic matrix tablets and erodible (hydrophobic) matrix tablets are the two most common types of solvent activated matrix tablets.

**2. Gel-forming hydrophilic matrix tablets:**

The medication is disseminated in a swellable hydrophilic polymer in gel-forming hydrophilic or swellable matrix systems, which can be homogeneous or heterogeneous. Researchers have been studying these systems extensively because they allow for consistent drug administration over a long period of time. The properties of the polymer influence drug release. The hydrophilic polymer in gel-forming hydrophilic matrix tablets is plasticized by the aqueous gastro intestinal fluid, causing macromolecular chain relaxation volume expansion. As a result of the gastro intestinal fluids penetrating the pill, a distinct front may be seen that distinguishes a dry, glassy core from a hydrated and rubbery gel coating. The dissolved drug diffuses through the swelling gel layer, causing a burst effect, which is generated by the dissolving and leaching of drug particles present on the surface prior to the development of the release controlling gel.

The relative position of the rubber glass interface, the rate at which it penetrates the tablet, the drug's diffusion coefficient, and the gel's erosion rate determine the mechanism of drug release from swellable devices. When the penetration rate is high relative to the drug diffusion rate through the swelling gel layer, the diffusion rate of the drug through the gel layer controls release, resulting in a diffusion regulated (Fickian) release mechanism. If drug diffusion through the gel layer is faster than water penetration, the integrated drug's release is governed by the interface's penetration rate, and zero order drug release with a constant release rate can be obtained. To define drug release from swelling controlled dosage forms, several dimensionless metrics have been proposed. The Deborah number ( $De$ ) represents the ratio of the Characteristic relaxation time of the swelling polymer relative to the characteristic diffusion time of the water into the polymer. The swelling interface number ( $Sw$ ) represents the ratio of the solvent penetration front velocity ( $v$ ) to the rate of drug diffusion through the swollen polymer:

$$De = \tau / t \quad Sw = v \cdot \delta (t) / ID$$

Where  $D$  is the diffusion coefficient of the drug in the swollen layer and  $\delta(t)$  is the thickness of the latter. In order to characterize release behavior, it is necessary to determine both  $D$  and  $S_w$  since neither of these values is sufficient by it. Peppas and co-workers have extensively investigated diffusion and solvent controlled drug release from swellable polymeric devices with various geometries. Release from swellable tablets can easily be analyzed by the following simple equation:

$$M_t / M_\infty = kt^n$$

Where  $M_t / M_\infty$  are the fractional drug release,  $k$  is a constant representing structural and geometrical characteristic of the device, and  $n$  gives the type of release mechanism.

When the rate at which the penetration front moves inward into the glassy core is high as compared to the diffusion rate of dissolved drug molecules through the swollen gel layer, release is controlled by the diffusion rate of the drug through the gel layer and a Fickian diffusion controlled release mechanism with  $n = 0.5$  is observed. If diffusion of

The drug through the gel layer is fast as compared to the solvent penetration rate, release of the incorporated drug is governed by the penetration rate of the interface. For dosage forms with slab geometry, this leads to zero-order release ( $n=1$ ), which is also called non-Fickian, case II or solvent penetration controlled release.

Release

Profiles with intermediate  $n$ -values ( $0.5 < n < 1$ ) are classified as anomalous. Other swellable polymers, which have

been applied in swelling controlled oral drug delivery systems, which show solvent controlled release, are guar gums, poly (ethylene oxide) (PEO), poly (vinyl alcohol), ethylene vinyl alcohol copolymers (EVA) and dextrans.

### 3. Erodible matrix tablets:

Another potential material platform for zero order drug release is erodible polymers such as polyanhydrides. Polyanhydrides, like various HPMC grades, generate a gel layer that erodes at a specified rate when exposed to water. The thickness of the gel Layer may remain constant over time if the correct polymer composition is used, resulting in a consistent release rate until the medication is depleted. [1, 8,9]

## XVI. EVALUATION TEST FOR SUSTAINED RELEASE MATRIX TABLETS:

### 1) Weight variation test -

To study weight variation, twenty tablets of the prepared formulation were weighed using an electronic balance and the average weight is calculated and the test was performed according to the official method.

2) **Uniformity of weight** - Every individual tablet in a batch should be of uniform weight and weight variation in within permissible limits. The weights were determined to within  $\pm 1$ mg. Weight control is based on a sample of 20 tablets.

### 3) Dimensions -

The dimensions (diameter and thickness) were then determined to within  $\pm 0.01$  mm by using digital Vernier calipers.

### 4) Hardness -

The hardness of the tablets was determined by diametric compression using a Hardness testing apparatus (Monsanto Type). A tablet hardness of about 4-5 kg is considered adequate for mechanical stability.

### 5) Friability -

The friability of the matrix tablets was measured by a Roche Friabilator. Tablets of a known weight ( $W_0$ ) or a sample of tablets is dedusted in a drum for a fixed time (100 revolutions) and weighed ( $W$ ) again. Permitted friability limit is 1 % w/w. Percentage friability was calculated from the weight loss by the following equation.

$$\% \text{ Friability} = \frac{W_0 - W}{W_0} \times 100$$

### 6) In-vitro dissolution study -

The release rate of matrix tablet was determined using United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml solvent and set RPM. A sample of the solution was withdrawn from the dissolution apparatus at different time interval. The samples were replaced with fresh dissolution medium of the same quantity. The samples were filtered through a membrane filter. The absorbance of these solutions was measured using a UV is double beam spectrophotometer.[4,21]

## XVII. CONCLUSION:

As a result of the above explanation, it is easy to deduce that sustained-release formulations are beneficial in enhancing dose efficiency as well as their effectiveness. Compatibility with the patient is also improving. Furthermore, all of this is available at a fair price. The dosage form is simple to adjust and very effective. In the case of antibiotics, where irrationality is a problem, this is useful. The employment of the same could lead to resistance.

## CONFLICTS OF INTEREST

There are no conflicts of interest and disclosures regarding the manuscript.

## ACKNOWLEDGEMENT

The authors express their sincere gratitude to K. B. H. S. S. Trust's Institute of Pharmacy, University Libraries, and all other sources for their cooperation and advice in writing this review.

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